

## REMARKS

Claims 1-96, 99-108 and 111-207 appear in this application for the Examiner's review and consideration.

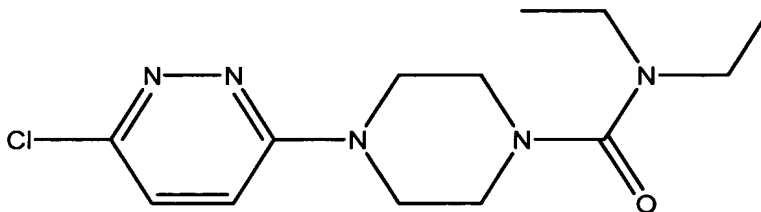
Applicants note with appreciation that, pursuant to item 2 on page 2 of the Office Action, the rejection of claims 42, 43, 45, 59 and 63 under 35 U.S.C. §103(a) has been withdrawn. Applicants also note with appreciation that the Office Action Summary and page 5, item 6 of the Office Action indicate that claims 21-60, 62, 63, 85-89, 99-101, 111 and 144-207 are allowed. Applicants further note that claims 2-17, 20 and 112-143 are not rejected but objected to.

Favorable reconsideration of the claims in view of the remarks herein is respectfully requested.

### REJECTION OF CLAIMS 1, 18, 19 AND 61 UNDER 35 U.S.C. §103(a)

On page 3, item 4 of the Office Action, claims 1, 18, 19 and 61 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over the publication of Toldy et al., *Acta Chimica Academiae Scientarum Hungaricae* 69(2):221-227 (1971) ("Toldy II").

The Office Action alleges, on page 3, that Toldy II teaches 4-(6-chloropyridazin-3-yl)-N,N-diethylpiperazine-1-carboxamide, i.e., the following compound:



and that this compound is "almost the same as applicants when applicant's formula (III) (*sic*; formula (I)?) has the following substituents:  $R^1 = \text{Cl}$ ;  $n = m = 0$ ;  $A = \text{NH}$ ; and  $R^4 = \text{ethyl}$ ."

Applicants respectfully traverse.

Preliminarily, Applicants note that an English translation of a Toldy reference, NOT Toldy II but *Acta Chim. (Budapest)* 70(1-2):101-122 (1971) of Toldy et al. was provided in error with the Office Action. This was discussed with Examiner Habte thereafter; records of that discussion appear in Examiner Habte's Interview Summary of May 1, 2006 and in Applicants' Statement Of The Substance Of The Interview of May 12, 2006. On or about

August 2, 2006 Examiner Habte arranged for an English language translation of Toldy II ("Toldy IIE") to be provided to Applicants, for which they express appreciation. Therefore, Applicants have based their remarks below on the USPTO-provided Toldy IIE and not on the German-language Toldy II.

**1. The Legal Standard to Establish a *Prima Facie* Case of Obviousness**

The Examiner has the burden of establishing a *prima facie* case of obviousness by proving three elements: (1) a particular reference (or combined references) must suggest or teach all the limitations of the challenged claim, (2) a suggestion or motivation from the prior art or in the knowledge generally available to one of ordinary skill in the art to modify or combine the reference teachings, and (3) a reasonable expectation of success must exist from the prior art. M.P.E.P. §§2142, 2143, citing *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Further, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." M.P.E.P. 2141.02(VI) (emphasis in original) (Citing *W.L. Gore & Associates, Inc. v. Garlock*, 721 F.2d 1540 (Fed. Cir. 1983)).

**2. Toldy IIE Fails to Teach or Suggest Each and Every Claim Element**

Toldy IIE discloses, in the second paragraph on page 2, that "alkoxyphenyl isothiocyanates and N-substituted piperazines" can be reacted to obtain "thiocarbamide derivatives". The exemplary N-substituted piperazines that are taught in Toldy IIE are:

- N-carbethoxy piperazine,
- N-carbo-n-propoxy piperazine,
- N-carbo-i-propoxy piperazine, and
- N-carbo-i-amyloxy piperazine

(top portion of page 6 of Toldy IIE). Additional N-substituted piperazines are purportedly provided in Table I of Toldy IIE (see line following "Method A" on page 5 of Toldy IIE). However, no such table can be found within the boundaries of Toldy IIE. In contrast, the piperazine moiety of the compounds of, e.g., independent claim 1, is substituted with pyridazine. Because there is no disclosure in Toldy IIE of a piperazine that is substituted with pyridazine, Toldy IIE fails to teach or even suggest all elements of the rejected claim 1, and the rejected claims dependent therefrom.

Applicants note that an earlier publication in the "Toldy" series, i.e., Solym et al. and Toldy, "Thiokarbamidderivate mit tuberkulostatischer Wirkung, I Verbindungen mit heterocyklischem thiokarbamidskelett," *Acta Chimica Academiae Scientiarum Hungaricae, Tomus 68*(1-2):99-132 (1971) ("Toldy I") and the English translation thereof, references C32 and C33 respectively in the Supplemental Information Disclosure Statement which accompanied the Amendment filed on February 16, 2006, unlike Toldy IIE, clearly do provide copies of the tables referred to therein. However, missing Table I of Toldy IIE cannot correspond to Table I of Toldy I because, *inter alia*, the former requires 21 compounds ("I-XXI," line following "Method A" on page 5 of Toldy IIE) while the latter provides only 14 compounds (e.g., Table I of reference C33).

Given that there is no Table I in Toldy IIE, Applicants submit that there is no compound 4-(6-chloropyridazin-3-yl)-N,N-diethylpiperazine-1-carboxamide disclosed, or even suggested, in Toldy IIE as is alleged in the Office Action.

**3. Toldy IIE Teaches Against the Substitution of Piperazine with Substituents Other Than Carbalkoxy Substituents**

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. *In re Gurley*, 27 F.3d 551, 31 U.S.P.Q.2d 1130 (Fed. Cir. 1994).

As discussed above, Toldy IIE discloses at page 2 that alkoxyphenyl isothiocyanates can be reacted with N-substituted piperazines. Toldy IIE further discloses at page 2 that the majority of the resulting thiocarbamide derivatives are inactive, and that only those thiocarbamide derivatives with a carbalkoxy substituent formed an exception, i.e., had activity. The compounds of claim 1, however, are substituted with pyridazine. Thus, since Toldy IIE teaches against the substitution with substituents other than carbalkoxy, Toldy IIE does not render the claimed compounds obvious. "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." M.P.E.P. 2141.02(VI) (emphasis in original) (Citing *W.L. Gore & Associates, Inc. v. Garlock*, 721 F.2d 1540 (Fed. Cir. 1983)).

## CONCLUSION

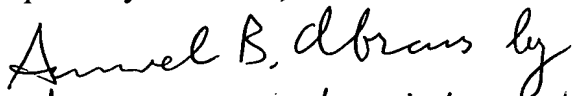
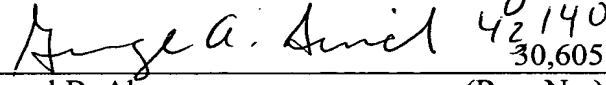
Applicants respectfully submit that Toldy IIE fails to teach or suggest all of the claim limitations, as discussed in detail above. Furthermore, Applicants respectfully submit that there is no suggestion or motivation from the prior art to modify the teachings of Toldy IIE to include, *inter alia*, a 3-pyridazinyl group, as is recited in present independent claim 1. Additionally, even if only for the sake of argument such modifications were to be made, Applicants respectfully submit that Toldy IIE does not and cannot indicate any reasonable expectation of success to one of ordinary skill in the art in connection with the invention claimed in claim 1 and the claims dependent therefrom.

Accordingly, as the compounds recited in independent claim 1, and claims 18, 19 and 61 dependent therefrom, are not obvious over the teachings of Toldy IIE for at least these reasons, reconsideration and withdrawal of the rejection relating thereto and early allowance of these claims is respectfully requested.

Applicants believe that no fee is due in connection with this amendment (other than for the Petition for Extension of Time). However, should the Patent Office determine that a fee is due, please charge the required amount to Jones Day Deposit Account 50-3013.

Respectfully submitted,

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Enclosures